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Higher Levels of Stress Are Associated with a Significant Symptom Burden in Oncology Outpatients Receiving Chemotherapy

Author
Jakovljevic, Katarina

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by

Katarina Jakovljevic

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Approved:

DocuSigned by:
Christine Miaskowski
4058DA2CA6554BB...

Christine Miaskowski

Chair

DocuSigned by:
Kord Kober

Kord Kober

DocuSigned by:
Astrid Block
DA5943871E08415...

Astrid Block

Committee Members

Abstract

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by Katarina Jakovljevic

Background: A cancer diagnosis and associated treatments, as well as the uncertainty of the disease course, are stressful experiences for most patients. However, little information is available on the relationship between stress and symptom burden. The study purpose was to evaluate for differences in the severity of fatigue, lack of energy, sleep disturbance, and cognitive function, among three groups of patients with distinct stress profiles.

Methods: Patients receiving chemotherapy (n=957) completed measures of general, cancer specific, and cumulative life stress and symptom inventories. Latent profile analysis was used to identify subgroups of patients with distinct stress profiles.

Results: Three distinct subgroups of patients were identified (i.e., Stressed (39.3%), Normative (54.3%), Resilient (5.7%)). For cognitive function, significant differences were found among the latent classes (Stressed<Normative<Resilient). For both sleep disturbance and morning and evening fatigue, compared to the Normative and Resilient classes, the Stressed class reported higher severity scores. Compared to the Normative and Resilient classes, the Stressed class reported low levels of morning energy. Compared to the Normative class, the Stressed class reported lower levels of evening energy.

Conclusions: Consistent with our a priori hypothesis, patients in the Stressed class had the highest symptom severity scores for all four symptoms and all of these scores were above the clinically meaningful cutoffs for the various instruments.

Table of Contents

List of Tables

Introduction

A cancer diagnosis, its related treatments, and the uncertainty of the disease course are stressful experiences for most patients[1, 2] that can have acute and chronic effects.[3] Stress is an adaptive response that activates the sympathetic and parasympathetic nervous systems as well as the hypothalamic-pituitary-adrenal (HPA) axis.[4] While the types and the duration of stressors vary greatly, equally important is the significant amount of variability in individuals' cognitive, emotional, and neurobiological responses to stress.[5] A growing body of preclinical and clinical evidence, summarized below, suggests that these inter-individual differences in oncology patients' responses to stress may contribute to the occurrence and severity of common physical symptoms (i.e., fatigue, sleep disturbance, deficits in energy levels, cognitive impairment) associated with the receipt of chemotherapy (CTX).

Fatigue occurs in up to 90% of patients undergoing CTX.[6] In the general population, fatigue is an adaptive response to acute stress that assists an individual to conserve energy and maintain homeostasis. In situations of chronic stress or cumulative exposure to stressful life events, the sympathetic nervous system (SNS), parasympathetic nervous system (PNS), and HPA axis experience an increased allostatic load which results in increases in fatigue severity.[7] In terms of oncology patients, in a recent review,[2] the authors hypothesized that stress-induced increases in inflammatory responses were an underlying mechanism for fatigue. However, only one study was identified that evaluated for associations between fatigue severity and stress in oncology patients receiving CTX. In this study, that used latent profile analysis (LPA) to identify subgroups of patients with distinct morning and evening fatigue profiles,[8] higher levels of general and disease-specific stress were reported by patients in the highest morning and evening fatigue subgroups.

Sleep disturbance is reported by 30% to 88% of oncology patients and has a significant impact on patients' mood, functional status, and quality of life.[9, 10] As noted in two recent reviews,[3, 11] findings from several animal and human studies suggest that stress can have an impact on the sleep-wake cycle in a variety of ways depending primarily on the types of stressors experienced, the duration of exposure (i.e., acute versus chronic stress), and inter-individual responses to stress. However, research on the association between sleep disturbance and stress in oncology patients in extremely limited. In the only study identified,[12] that evaluated twenty-nine newly diagnosed patients with breast cancer and co-occurring insomnia, while no measure of stress was used, patients with insomnia prior to their cancer diagnosis reported high cognitive pre-sleep arousal scores (i.e., a proxy measure of stress).

Cancer-related cognitive impairment (CRCI) is highly prevalent with up to 75% of patients reporting decrements in cognition during CTX.[13] In an excellent review,[14] Datta and Arnsten describe the influences of chronic stress on the functioning of the prefrontal cortex (PFC). Findings across studies suggest that this area of the brain, that controls behaviors, thoughts, and emotions, when exposed to chronic stress exhibits changes in connectivity and neuronal atrophy. It is interesting to note that in a recent magnetic resonance imaging (MRI) study of forty patients with breast cancer,[15] CRCI was associated with changes in functional connectivity in the PFC. In addition, findings from a systematic review suggest that psychosocial factors, including increased stress, are associated with CRCI.[16] Finally, in a study of patients undergoing CTX,[17] higher levels of CRCI were associated with higher levels of general and disease specific stress.

Given the high levels of stress that oncology patients experience; the growing preclinical evidence, as well as evidence from the general population, on the associations between stress and

common physical symptoms; and the paucity of research on these associations in oncology patients, in this study we extend our previous work on stress in oncology patients. This study is a logical extension of our previous report that identified distinct stress profiles in a large sample of oncology patients undergoing CTX (n=957).[18] In brief, we used LPA to identify subgroups of patients based on their concurrent evaluations of global (i.e. Perceived Stress Scale [19]) and cancer-specific stress (i.e., Impact of Event Scale-Revised [20]), lifetime stress exposure (i.e., Life Stressor Checklist-Revised [21]), and resilience (i.e., Connor-Davidson Resilience Scale [22]). Three subgroups of patients with distinct stress profiles were identified (Table 1). The first group, labeled "Normative" (54.3%), was characterized by intermediate levels of global stress and resilience, lower levels of cancer-related stress, and the lowest amount of cumulative life stress. The second group, labeled "Stressed" (39.3%) reported the highest levels of global and cancer specific stress, the lowest resilience scores, and the most life stress. The third group, labeled "Resilient" (5.7%) had the lowest global stress scores, levels of cancer-specific stress that were comparable to the "normative" group, the highest resilience scores, and intermediate levels of cumulative life stress. The purpose of this study was to evaluate for differences in the severity of fatigue, lack of energy, sleep disturbance, and cognitive function, among these three stress groups. We hypothesized that compared to patients in the other two groups, patients in the "stressed" group would have the highest physical symptom severity scores.

Methods

Patients and Settings

This analysis used data from a descriptive, longitudinal study that evaluated the symptom experience of oncology outpatients receiving CTX.[23] Eligibility criteria included: ≥18 years of age; diagnosis of breast, gastrointestinal, gynecological, or lung cancer; received CTX within the

preceding four weeks and scheduled to receive two additional cycles; and able to read, write, and understand English. Recruitment occurred at two Comprehensive Cancer Centers, one Veteran's Affairs hospital, and four community-based oncology clinics. Written informed consent was obtained from all patients. Study procedures were approved by the Committee on Human Research at the University of California, San Francisco and by each study site. Of the 2234 patients approached, 1343 consented to participate (60.1%). Patients who completed all of the stress and resilience measures (n=957) were included in this analysis.

Instruments

Demographic and Clinical Characteristics - Patients completed a demographic questionnaire, the Karnofsky Performance Status (KPS) scale,[24] and the Self-Administered Comorbidity Questionnaire (SCQ).[25] Medical records were reviewed for disease and treatment information.

Stress and Resilience Measures

Perceived Stress Scale (PSS) - The 14-item PSS was used to assess global stress. [19] Patients indicated the degree to which they perceived life circumstances as stressful over the previous week. Items were rated from 0 (never) to 4 (very often). Higher sum scores indicate greater perceived stress. The PSS has well established validity and reliability.[19] In this current study, its Cronbach's alpha was 0.89.

Impact of Event Scale-Revised (IES-R) - The IES-R is a 22-item instrument that was used to measure distress associated with cancer and its treatment.[20] Patients rated each item based on how distressing each potential difficulty was for them during the past week "with respect to their cancer and its treatment". Each item was rated on a 0 to 4 Likert scale (i.e., 0 = not at all, 1 = a little bit, 2 = moderately, 3 = quite a bit, 4 = extremely). Three subscales were created using the mean of the responses. A total IES-R score was created by summing the

responses to the 22 items. The three subscales evaluate the levels of intrusion, avoidance, and hyperarousal perceived by a patient. The total IES-R score can range from 0 to 88. For the total IES-R score, a sum score of ≥24 indicates clinically meaningful post-traumatic symptomatology and scores of ≥33 indicate probable PTSD.[26, 27] The IES-R has well established validity and reliability.[26] In the current study, its Cronbach's alpha was 0.92.

Life Stressor Checklist-Revised (LSC-R) - The 30-item LSC-R was used to evaluate lifetime exposure to stressful life events.[21] Patients indicated the occurrence of 30 stressors and rated the effect of each stressor on their past year of life, from 1 (not at all) to 5 (extremely). A higher number (i.e., count) of stressful life events and higher mean effect scores indicate greater stress exposure and impact, respectively. LSC-R demonstrates adequate test–retest reliability and criterion-related validity among diverse populations. [28, 29]

Connor-Davidson Resilience Scale (CD-RISC-10) - The 10-item CD-RISC-10 was used to measure resilience.[22] Items were rated from 0 (not true at all) to 4 (true nearly all the time). Higher sum scores indicate greater resilience. CD-RISC-10 has adequate validity and reliability in diverse populations.[22, 30] In the current study, its Cronbach's alpha was 0.90.

Symptom Measures

Attentional Function Index (AFI) – The 16-item AFI was designed to measure attentional function.[31] A higher total mean score on a 0 to 10 NRS indicates greater capacity to direct attention.[31] Total scores are grouped into categories of attentional function (i.e., <5.0 low function, 5.0 to 7.5 moderate function, >7.5 high function).[32] In addition, the AFI has three subscales (i.e., effective action, attentional lapses, interpersonal effectiveness). The AFI has well established reliability and validity.[31] In this study, the Cronbach's alpha for the total AFI score was 0.93.

General Sleep Disturbance Scale (GSDS) – The 21-item GSDS was designed to assess the quality of sleep in the past week.[33] Each item was rated on a 0 (never) to 7 (everyday) NRS. The GSDS total score is the sum of the seven subscale scores that can range from 0 (no disturbance) to 147 (extreme sleep disturbance). Each mean subscale score can range from 0 to 7. Higher total and subscale scores indicate higher levels of sleep disturbance. Subscales scores of ≥3 and a GSDS total score of ≥43 indicate a significant level of sleep disturbance.[34] The GSDS has well-established validity and reliability.[33, 35, 36] In the current study, the Cronbach's alpha for the GSDS total score was 0.83.

Lee Fatigue Scale (LFS) – The 18-item LFS is designed to assess physical fatigue and energy.[37] Each item was rated on a 0 to 10 numeric rating scale (NRS). Total fatigue and energy scores are calculated as the mean of the 13 fatigue items and the 5 energy items, respectively. Higher scores indicate greater fatigue severity and higher levels of energy. Using separate LFS questionnaires, patients were asked to rate each item based on how they felt within 30 minutes of awakening (i.e., morning fatigue, morning energy) and prior to going to bed (i.e., evening fatigue, evening energy). The LFS has established cut-off scores for clinically meaningful levels of fatigue (i.e., ≥3.2 for morning fatigue, ≥5.6 for evening fatigue) (34) and energy (i.e., ≤6.2 for morning energy, ≤3.5 for evening energy).[34] It was chosen for this study because it is relatively short, easy to administer, and has well established validity and reliability.[36-41] In the current study, the Cronbach's alphas were 0.96 for morning and 0.93 for evening fatigue and 0.95 for morning and 0.93 for evening energy.

Data Analysis

As described previously,[18] LPA was used to identify subgroups (i.e., latent classes) of patients with distinct stress profiles, using patients' scores on the stress (PSS, IES-R, LSC-R)

and resilience (CD-RISC-10) measures. LPA was conducted using MPlus™ Version 7.4.[42] Estimation was conducted using robust maximum likelihood and the expectation maximization algorithm. Statistical fit indices were used to determine the number of classes that best captured variability, while maintaining conceptual clarity.[43, 44]

For this analysis, descriptive statistics and frequency distributions were calculated for demographic and clinical characteristics, stress and resilience scores, using SPSS version 26.[45] Analyses of variance, Kruskal-Wallis, or Chi-square analyses were used to evaluate for differences in demographic and clinical characteristics and symptom scores among the classes. A p-value of <0.05 were considered statistically significant. The Bonferroni correction was used for post hoc contrasts.

Results

Results of the LPA

The LPA identified three latent classes based on the stress and resilience measures.[18] Supplemental Table 1 displays the fit indices for the 1- through 4-class solutions. The 3-class solution was selected based on its lower Bayesian Information Criterion, higher entropy, and statistically significant Vuong-Lo-Mendell-Rubin, indicating the best fit.

Of the entire sample, 382 patients (39.9%) were classified as “Stressed”, 520 patients (54.3%) as “Normative”, and 55 patients (5.7%) as “Resilient”. To name these classes (Table 1), mean stress and resilience scores were compared among the classes, as well as to established cut-off scores[26] and national normative data.[22, 46] The latent classes differed significantly on all of the stress and resilience scores (all $p<0.001$). Post hoc contrasts revealed consistent patterns for global stress (i.e., PSS; Stressed > Normative > Resilient) and resilience (Stressed < Normative < Resilient). For occurrence of life stressors measured using the LSC-R, post hoc contrasts

revealed the following pattern: Stressed > Resilient > Normative. For cancer-related stress, Stressed patients reported higher IES-R total scores than Normative and Resilient patients (i.e., Stressed > Normative and Resilient).[18]

Differences in Demographic and Clinical Characteristics

As shown in Supplemental Table 2,[18] compared to Normative patients, Stressed patients were younger, more likely to be female, had fewer years of education, lower annual household incomes, and were less likely to be employed. Compared to Normative and Resilient classes, Stressed patients were more likely to be single and live alone.

For clinical characteristics, functional status, comorbidities, as well as self-reported depression and back pain differed among the latent classes. Compared to Normative patients, Stressed patients reported a higher comorbidity burden and were more likely to report back pain. Compared to Normative and Resilient patients, Stressed patients had lower functional status scores and were more likely to report depression. Demographic and clinical characteristics did not differ between Normative and Resilient patients. Moreover, no disease or treatment characteristics differed among the classes.

Differences in Symptom Severity Scores

As shown in Table 2, for attentional function, significant differences in the interpersonal effectiveness and total AFI scores were found among the latent classes (Stressed < Normative < Resilient). In addition, compared to the other two classes, patients in the stressed class had lower effective action and attentional lapses subscale scores.

For sleep disturbance, as well as morning and evening fatigue, compared to the Normative and Resilient classes, patients in the Stressed class reported higher GSDS and LFS scores. For morning energy, compared to the Normative and Resilient classes, patients in the

Stressed class reported low scores. For evening energy, compared to the Normative class, patients in the Stressed class reported lower scores.

Discussion

This study is the first to evaluate for differences in fatigue, energy levels, sleep disturbance, and cognitive function in subgroups of patients with distinct stress profiles. Details on the differences among these subgroups in terms of their specific stress profiles, as well as demographic and clinical characteristics are described in our previous publication.[18] The remainder of this discussion focuses on our findings related to differences among the subgroups in the severity of common physical symptoms associated with cancer and CTX administration.

Consistent with our a priori hypothesis, patients in the Stressed class had the highest symptom severity scores for all four symptoms and all of these scores were above the clinically meaningful cutoffs for the various instruments. In contrast, while the stress and resilience scores differed between the Normative and Resilient classes, for most of the symptoms, no between group differences in symptom severity scores were found. This finding may be related to the relatively high symptom burden experienced by all three classes or the relatively small number of patients in the Resilient class.

While numerous studies have investigated risk factors for CRCI during and following cancer treatment,[47-50] the majority have evaluated for associations with demographic, clinical, and treatment characteristics using a variety of subjective and objective measures. In this study and consistent with previous reports,[16] we provide additional evidence that a subgroup of oncology patients with high levels of general and disease-specific stress, as well as cumulative life stress have the worse decrements in cognitive function. While the total scores and the interpersonal effectiveness subscale scores of the AFI differentiated among the three classes, all

three subgroups had moderate decrements in cognitive function. The AFI evaluates patients' perceptions of their effectiveness in carrying out basic activities of daily living that require focused attention; their perceived difficulties in directing attention on daily tasks, as well as their perceptions of their ability to interact in a deliberate manner that depends on selective attention.[31] Of note, in a recent functional MRI study, that evaluated patients with breast cancer undergoing CTX,[51] decreases in AFI scores paralleled disruptions in resting-state BOLD functional connectivity in parietal and frontal brain regions. To confirm the previous observations that chronic stress effects the functioning of the PFC,[14] future studies of CRCI should include both subjective and objective measures of cognitive function as well as multidimensional measures of stress.

In terms sleep disturbance, while the three latent classes had total sleep disturbance scores about the clinically meaningful cutoff, patients in the Stressed class had scores that represent an extremely high level of sleep disturbance that is comparable to scores reported by shift workers (i.e., 60.5)[33] and parents of newborn infants (55.5).[38] In terms of the GSDS subscale scores, the high levels of mid-sleep and early awakenings suggest that all three classes have problems with sleep maintenance. Of note, for patients in the Stressed class, all of the GSDS subscale scores were above the clinically meaningful cutoff of $\geq$3 days per week. In particular, their score of 3.6 ($\pm$2.3) on the sleep onset latency subscale suggests that these patients have problems with both sleep initiation and maintenance. Again, our findings are consistent with the preclinical and human studies of the negative impact of stress on sleep.[3, 11]

Previous research from our group has demonstrated that morning and evening fatigue are distinct but related symptoms.[23, 52, 53] Based on the scores reported by our Stressed class, high levels of general and disease specific stress, as well as cumulative life stress are associated with

clinically meaningful levels of both morning and evening fatigue. While lack of energy and fatigue are used interchangeably in the symptom literature, a growing body of evidence suggests that energy and fatigue are distinct but related symptoms.[54-56] While no studies have evaluated for associations between decrements in energy levels and stress, while our Stressed class reported decrements in both morning and evening energy levels, the other two classes reported morning energy levels that were well below the clinically meaningful cutoff of $\leq$6.2. These findings may be related to the relatively high levels of sleep disturbance in all three classes and warrant confirmation in future studies.

Consistent with our a priori hypothesis, patients in the Stressed class reported the highest level of symptom burden. Of note, the patients in this subgroup (i.e., 41% of the sample) reported clinically meaningful levels of all four of these co-occurring symptom. This extremely high risk group was younger, more likely to be female, had a lower socioeconomic status, was not married or partnered, was more likely to live alone, had a poorer functional status, and a worse comorbidity profile (see Supplementary Table 2).[18] These high risk patients warrant ongoing assessments of both stress and symptom burden.

While this study has several limitations, it provides directions for future research. While the sample was heterogeneous in terms of cancer diagnoses and CTX regimens, it was fairly homogenous in terms of gender, educational level, and ethnicity. Given that the stress measures were done only once, changes in the severity of stress and symptoms could not be evaluated. Future longitudinal studies, that use analytic techniques like parallel process growth modeling,[57] will be able to discern the causal relationships between stress and symptom burden. While recent investigations in symptoms science are focused on an evaluation of multiple co-occurring symptoms and symptom clusters in oncology patients and patients with other chronic conditions,

[58, 59] as noted in the introduction to this paper, the limited amount of research has focused on an examination of the relationships between stress and single symptoms. Given the findings from this study, careful consideration should be given to an evaluation of not only general, disease-specific, and cumulative life stress but multiple co-occurring symptoms in patients with cancer and other chronic conditions. These types of studies that include both subjective and objective measures, as well as biomarkers will increase our knowledge of the fundamental mechanisms that underlie the relationships between stress and symptoms.

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Table 1 – Differences Among the Latent Classes in the Stress Profile Measures

Characteristic	Stressed (1) 39.9% (n = 382)	Normative (2) 54.3% (n = 520)	Resilient (3) 5.7% (n = 55)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Perceived Stress Scale	25.4 (6.7)	14.2 (5.0)	8.5 (4.5)	F=502.26, p<.001 1>2>3
Impact of Event Scale-Revised (IES-R) total score	27.9 (13.8)	12.0 (7.0)	15.4 (12.1)	F=244.85, p<.001 1>2 and 3
Life Stressor Checklist-Revised (LSC-R) total score	8.0 (4.7)	4.6 (2.4)	6.2 (4.2)	F=92.34, p<.001 1>3>2
Connor Davidson Resilience score	25.7 (6.4)	32.2 (4.2)	39.7 (0.5)	F=276.40, p<.001 1<2<3

Abbreviation: SD = standard deviation

Table 2 – Differences in Symptom Characteristics Among the Stress Latent Classes

Characteristic	Stressed (1) 39.9% (n = 382)	Normative (2) 54.3% (n = 520)	Resilient (3) 5.7% (n = 55)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Attentional function	5.4 (1.6)	7.0 (1.6)	7.7 (1.5)	F = 135.70, p < .001 1 < 2 < 3
Sleep disturbance	61.4 (19.6)	45.6 (18.1)	48.4 (21.6)	F = 75.58, p < .001 1 > 2 and 3
Morning fatigue	4.1 (2.4)	2.4 (1.9)	2.4 (2.0)	F = 73.21, p < .001 1 > 2 and 3
Evening fatigue	5.8 (2.1)	5.0 (2.0)	4.5 (2.3)	F = 18.37, p < .001 1 > 2 and 3
Morning energy	3.9 (2.1)	4.7 (2.2)	4.9 (2.5)	F = 18.62, p < .001 1 < 2 and 3
Evening energy	3.2 (2.0)	3.8 (1.9)	3.9 (2.3)	F = 9.24, p < .001 1 < 2

Abbreviations: NS = not significant, SD = standard deviation

Supplemental Table 1 - Latent Profile Solutions and Fit Indices for One Through Four Class Solutions

Model	LL	AIC	BIC	Entropy	VLMR
1 Class	-3607.97	7243.93	7312.03	n/a	n/a
2 Class	-3446.31	6950.63	7091.68	.56	323.31****
3 Class[a]	-3390.00	6868.01	7082.01	.73	112.62****
4 Class	-3349.51	6817.02	7103.98	.65	80.99ns

**** $p < .0001$

[a] The three class solution was selected because the BIC for that solution was lower than the BIC for both the 2- and 4-class solutions. In addition, the VLMR was significant for the 3-class solution, indicating that three classes fit the data better than two classes. The VLMR was not significant for the 4-class solution, indicating that too many classes had been extracted.

Abbreviations: AIC = Akaike's Information Criterion; BIC = Bayesian Information Criterion; LL = log-likelihood; n/a = not applicable, ns = not significant; VLMR = Vuong-Lo-Mendell-Rubin likelihood ratio test for the K vs. K-1 model.

Supplemental Table 2 – Differences in Demographic and Clinical Characteristics Among the Stress Latent Classes

Characteristic	Stressed (1) 39.9% (n = 382)	Normative (2) 54.3% (n = 520)	Resilient (3) 5.7% (n = 55)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)	56.2 (12.0)	58.2 (11.9)	59.7 (9.9)	F = 4.24, p = .015 1 < 2
Education (years)	15.9 (2.9)	16.4 (3.0)	16.3 (3.3)	F = 3.56, p = .029 1 < 2
Body mass index (kg/m^2)	26.5 (5.8)	26.0 (5.4)	27.1 (6.5)	F = 1.43, p = .241
Alcohol Use Disorders Identification Test score	3.2 (3.0)	2.7 (2.0)	2.9 (2.3)	F = 2.89, p = .057
Karnofsky Performance Status score	76.6 (12.4)	83.0 (11.5)	82.9 (12.0)	F = 31.42, p < .001 1 < 2 and 3
Self-administered Comorbidity Questionnaire score	6.2 (3.5)	5.0 (2.8)	5.2 (3.1)	F = 15.98, p < .001 1 > 2
Time since diagnosis (years)	2.3 (4.6)	2.1 (3.9)	1.6 (3.0)	KW, p = .222
Time since diagnosis (years, median)	0.45	0.42	0.36	
Number of prior cancer treatments	1.8 (1.5)	1.7 (1.5)	1.4 (1.4)	F = 1.33, p = .266
Number of metastatic sites including lymph node involvement [a]	1.3 (1.3)	1.2 (1.2)	1.4 (1.4)	F = 1.13, p = .324
Number of metastatic sites excluding lymph node involvement	0.8 (1.1)	0.8 (1.0)	0.8 (1.2)	F = 0.36, p = .697
Hemoglobin	11.5 (1.4)	11.6 (1.4)	11.7 (1.3)	F = 0.80, p = .448
Hematocrit	34.5 (4.1)	34.8 (4.2)	35.2 (3.7)	F = 1.10, p = .334
	% (n)	% (n)	% (n)	
Gender (% female)	85.1 (325)	74.4 (387)	78.2 (43)	X^2 = 15.03, p <.001 1 > 2
Self-reported ethnicity White Asian or Pacific Islander Black Hispanic, Mixed, or Other	 69.1 (260) 12.4 (46) 6.6 (25) 12.0 (45)	 73.0 (375) 12.5 (64) 7.0 (36) 7.6 (39)	 68.5 (37) 13.0 (7) 11.1 (6) 7.4 (4)	X^2 = 6.56, p = .364
Married or partnered (% yes)	55.8 (211)	70.5 (363)	83.6 (46)	X^2 = 29.30, p < .001 1 < 2 and 3
Lives alone (% yes)	26.5 (100)	18.9 (97)	10.9 (6)	X^2 = 11.34, p = .003 1 > 2 and 3
Currently employed (% yes)	26.8 (102)	40.8 (210)	29.1 (16)	X^2 = 19.55, p < .001 1 < 2

Characteristic	Stressed (1) 39.9 % (n = 382)	Normative (2) 54.3% (n = 520)	Resilient (3) 5.7% (n = 55)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Annual household income				
Less than $30,000	28.0 (97)	10.9 (50)	13.5 (7)	
$30,000 to $70,000	23.4 (81)	20.7 (95)	13.5 (7)	KW, p < .001
$70,000 to $100,000	16.5 (57)	17.9 (82)	15.4 (8)	1 < 2 and 3
Greater than $100,000	32.1 (111)	50.4 (231)	57.7 (30)	
Child care responsibilities (% yes)	23.0 (86)	21.8 (111)	15.1 (8)	$X^2 = 1.70$, p = .427
Elder care responsibilities (% yes)	9.4 (32)	6.7 (32)	7.8 (4)	$X^2 = 1.94$, p = .379
Exercise on a regular basis (% yes)	66.0 (247)	72.0 (373)	74.5 (41)	$X^2 = 4.29$, p = .117
Specific comorbid conditions				
Heart disease	5.8 (22)	4.4 (23)	7.3 (4)	$X^2 = 1.37$, p = .505
High blood pressure	31.2 (119)	29.8 (155)	38.2 (21)	$X^2 = 1.67$, p = .434
Lung disease	10.5 (40)	12.9 (67)	12.7 (7)	$X^2 = 1.26$, p = .533
Diabetes	9.9 (38)	7.3 (38)	12.7 (7)	$X^2 = 3.15$, p = .207
Ulcer or stomach disease	6.5 (25)	3.7 (19)	7.3 (4)	$X^2 = 4.49$, p = .106
Kidney disease	2.4 (9)	0.6 (3)	3.6 (2)	$X^2 = 6.75$, p = .034
				No significant pairwise contrasts
Liver disease	5.8 (22)	7.7 (40)	1.8 (1)	$X^2 = 3.49$, p = .174
Anemia or blood disease	14.9 (57)	11.7 (61)	7.3 (4)	$X^2 = 3.59$, p = .166
Depression	33.8 (129)	10.0 (52)	9.1 (5)	$X^2 = 83.45$, p < .001
				1 > 2 and 3
Osteoarthritis	13.6 (52)	11.0 (57)	14.5 (8)	$X^2 = 1.74$, p = .420
Back pain	33.0 (126)	20.0 (104)	23.6 (13)	$X^2 = 19.69$, p <.001
				1 > 2
Rheumatoid arthritis	3.4 (13)	3.1 (16)	7.3 (4)	$X^2 = 2.63$, p = .268
Cancer diagnosis				
Breast cancer	41.4 (158)	39.2 (204)	41.8 (23)	
Gastrointestinal cancer	28.8 (110)	31.0 (161)	30.9 (17)	$X^2 = 7.75$, p = .257
Gynecological cancer	20.2 (77)	15.8 (82)	20.0 (11)	
Lung cancer	9.7 (37)	14.0 (73)	7.3 (4)	
Prior cancer treatment				
No prior treatment	18.3 (69)	23.2 (118)	26.9 (14)	
Only surgery, CTX, or RT	44.7 (169)	42.8 (218)	42.3 (22)	$X^2 = 5.85$, p = .441
Surgery and CTX, or surgery and RT, or CTX and RT	21.2 (80)	21.4 (109)	21.2 (11)	
Surgery and CTX and RT	15.9 (60)	12.6 (64)	9.6 (5)	

Characteristic	Stressed (1) 39.9% (n = 382)	Normative (2) 54.3% (n = 520)	Resilient (3) 5.7% (n = 55)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Metastatic sites				
No metastasis	31.7 (120)	31.6 (164)	27.8 (15)	
Only lymph node metastasis	24.3 (92)	22.9 (119)	25.9 (14)	$X^2 = 6.06$, p = .417
Only metastatic disease in other sites	19.0 (72)	24.1 (125)	16.7 (9)	
Metastatic disease in lymph nodes and other sites	25.1 (95)	21.4 (111)	29.6 (16)	
Cycle length				
14 day cycle	37.4 (142)	43.3 (225)	48.1 (26)	
21 day cycle	55.0 (209)	50.6 (263)	38.9 (21)	$X^2 = 8.58$, p = .073
28 day cycle	7.6 (29)	6.2 (32)	13.0 (7)	

[a] Total number of metastatic sites evaluated was 9.

Abbreviations: CTX = chemotherapy, kg = kilograms, KW = Kruskal Wallis, m^2 = meters squared, RT = radiation therapy, SD = standard deviation

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